IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applic Application of: Nobutaka Wakamiya Serial No.: 10/054,536 Filed: January 22, 2002 Title: Recombinant Human Mannan-Binding Protein and Producing Method of the Same Group Art Unit: 1645 Examiner: Devi, Sarvamangala J. N. Attorney Docket No. 19036/36614A	I hereby certify that this paper is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on APRIL 6, 2005. Eric M. Brusca Reg. No. 52,664

DECLARATION OF NOBUTAKA WAKAMIYA

1. I am the inventor named in the above-identified patent application ("the patent application") and I am the inventor of the invention claimed therein. A copy of my curriculum vitae is attached as Exhibit 1. I am are familiar with the contents of the patent application and make this declaration for the U.S. Patent and Trademark Office (PTO) to provide information that may be relevant to examination of the application.

2. I understand that the U.S. PTO cited a publication, Ohtani et al., Column 1P127 in Annual Meeting Report, Congress of Japanese Society for Immunology, Vol. 27, p. 182, September 29, 1997, as alleged prior art to the patent application. The Ohtani et al. publication is in Japanese, and an English translation is attached as Exhibit 2.

3. I am a named co-author of the Ohtani et al. publication, and I am familiar with my contributions and the contributions of other co-authors to the work summarized in the publication. To the extent that the Ohtani et al. publication describes or suggests the invention claimed in the patent application, the description is a description of my invention, and not an invention of the other co-authors. I conceived of the project summarized in the Ohtani et al. publication and how to carry it out. The other co-authors of the publication worked under my direction and supervision and did not otherwise make a substantial contribution to the invention.

4. I further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (18 U.S.C. 1001), and may jeopardize the validity of the application or any patent issuing thereon.

Date: April 4, 2005 Signature: N Wakamiya
Nobutaka Wakamiya

CURRICULUM VITAE OF NOBUTAKA WAKAMIYA, M.D.

[Academic and Professional Background]

March 1980 Graduated from Hirosaki University, Faculty of Medicine, School of Medicine.

July 1980 Joined to Osaka Prefectural Hospital as Resident Pediatrician.

April 1982 Admitted to Doctor`s Course in Department of Pathology (Virus III) at Graduate School of Medicine, Osaka University.

March 1986 Graduated from the Doctor`s Course above. Earned a degree of Doctor of Medicine.

June 1986 Enrolled in Dana-Farber Cancer Institute, Harvard University as a Research Fellow.

Jan. 1988 Joined to Research Institute for Microbial Diseases, Osaka University as an Assistant Professor.

Nov. 2000 Joined Asahikawa Medical College as a Professor and Chairman (the present position).

[Specialized Field]

Biochemistry, Immunology and Microbiology

[Membership of Societies Belonged]

The Japanese Biochemical Society
The Japanese Society for Virology
The Japanese Society for Immunology
American Society for Microbiology (ASM)
American Association for Cancer Research (AACR)

[The Present Research Theme]

Biological Functions and Roles of Animal Lectin (Collectin) possessing Collagen Motifs.

[Recent Scientific Japanese Publications on Collectin]

(1) Wakamiya N. and Suzuki Y., `Collectin Families to be acted as Bio-Defensive Lectin`, PROTEIN, NUCLEIC ACID AND ENZYME, Vol.45, No. 5, pp.655-663 (2000).

(2) Wakamiya N. and Suzuki Y., `Novel Hemangioendotheliocyte Scavenger Receptor CL-P1`, SEIKAGAKU, Vol.73, No. 3, pp.205-208 (2001).

[Recent Scientific English Publications on Collectin]

1. Ohtani, K., Suzuki, Y., Eda, S., Kawai, T., Kase, T., Yamazaki, H., Shimada, T., Keshi, H., Sakai, Y., Fukuoh, A., Sakamoto, T., Wakamiya, N.: Molecular cloning of a novel collectin from liver (CL-L1). J. Biol. Chem. 274(19): 13681-13689, 1999.
2. Ohtani, K., Suzuki, Y., Eda, S., Kawai, T., Kase, T., Keshi, H., Sakai, Y., Fukuoh, A., Sakamoto, T., Itabe, H., Suzutani, T., Ogasawara, M., Yoshida, I., Wakamiya, N.: The membrane-type collectin CL-P1 is a scavenger receptor on vascular endothelial cells. J. Biol. Chem. 276(47): 44222-44228, 2001.

--**----**----**----**----**----**----**----**----**--

ARCO PATENT OFFICE

Bo-eki Bldg., 123 Higashi-machi, Chuo-ku, Kobe 650-0031; Japan
P.O.Box 3, Kobe Port, Kobe 651-0191, Japan
Phone +81-78-321-8822 / Fax +81-78-391-5791
URL http://www.arco.chuo.kobe.jp
E-Mail office@arco.chuo.kobe.jp

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Patent Application No. 10/054,536
Of NOBUTAKA WAKAMIYA

I, **Seung-Lim SUNG**, of ARCO PATENT OFFICE at 3rd Fl., Bo-eki Building, 123 Higashi-machi, Chuo-ku, Kobe 650-0031 JAPAN, declare that I am familiar with the Japanese and the English languages and, to the best of my knowledge and belief, the attached is a full, true, and faithful translation into English of **Column 1P127, In Annual Meeting Report, Congress of Japanese Society for Immunology, Vol.27, p.182, September 29, 1997** which is identical to "Otani et al., Nippon Men'eki Gokkai Soaki, Gakujutsu Shukai Kiroku 27: 182, 29 September 1997 (Original & English translation)" cited as Reference V of the Office Action mailed on October 6, 2004 in the U.S. Patent Application No. 10/054,536.

Signature: _____
Seung-Lim SUNG

Date: **March 8, 2005**

English Translation of Column 1P127
In Annual Meeting Report,
Congress of Japanese Society for Immunology,
Vol.27, p.182, September 29, 1997.

1P127; Biological Properties of and Mass Expression in Eucaryotic Cells of Human Mannan Binding Protein

Katsuki OHTANI[1], Yasuhiko SUZUKI[1], Soji EDA[1], Takao KAWAI[1], Tetsuo KASE[1], Takashi SAKAMOTO[2,3], Hidetoshi UEMURA[3], and **Nobutaka WAKAMIYA**[2]. [[1]Osaka Prefectural Institute of Public Health, [2]Research Institute for Microbial Diseases, Osaka University, and [3]Research and Development Center, Fuso Pharmaceutical Industries, Ltd.]

We have been taking interest in physiological activities of Human Mannan Binding Protein (hMBP) and are still continuing the study thereon. Physiological activities of hMBP have been reported as activation of a complement (lectin pathway), opsonin activity and so on. We have been performing the research directed specifically to the suppression activity of hMBP against viral infection, and have found under *in vitro* experiment system that they possess anti-influenza virus activity. Although we are planning as the next step to verify such *in vitro* results under *in vivo* experiment system, such *in vivo* system usually needs a large amount of homogenous MBP. Accordingly we tried at this time to construct a system for expressing hMBP in eucaryotic cells.

Expression vector pNOW1 employed at this time is identical to that which was employed for expressing bovine conglutinin and was reported in the last Annual Congress. Plasmid pNOW-hMBP was constructed by introducing cDNA of hMBP into this vector. Expression of hMBP was then tried by introducing the plasmid so constructed into CHO cells ($dhfr^-$). Among G418-resistance cell clones, there were strains which expressed hMBP at the concentration of 13.2 μg/ml. Gene amplification was then performed by cultivating such strains under the presence of methotrexate (MTX) and selecting

the particular cells which possess resistance to methotrexate. Such selection was firstly performed with 5 nM MTX. As a result thereof, there were strains which expressed hMBP at the higher concentration of 54.1μg/ml. Then, the biochemical properties of MBP so taken are similar to those of MBP separated from human serum. Further, it was also confirmed that such MBP possessed an activity to inhibit hemagglutination by influenza virus.

--**------**------**------**------**------**------**------**------**--